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REVIEW

Femtosecond IR Pump-Probe Spectroscopy of Nonlinear Energy Localization in Protein Models and Model Proteins

Peter Hamm

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Abstract This paper reviews our experimental and theoretical efforts toward understanding vibrational self-trapping of the amide I and N–H mode of crystalline acetanilide (ACN), other similar hydrogen-bonded crystals, as well as of model peptides. In contrast to previous works, we used nonlinear IR spectroscopy as the experimental tool, which is specifically sensitive to the anharmonic contributions of the intramolecular interactions (as the nonlinear IR response of set of harmonic oscillators vanishes exactly). Our work reconfirms the previous assignment of the two bands of the amide I mode of ACN as being a self-trapped and a free exciton state, but in addition also establishes the lifetimes of these states and identifies the relevant phonons. Furthermore, we provide evidence for vibrationally self-trapped states also in model α-helices. However, given the short lifetime, any biological relevance in the sense of Davydov's initial proposal can probably be ruled out.

Keywords Vibrational self-trapping · Acetanilide · Femtosecond · IR spectroscopy · Nonlinear spectroscopy

1 Introduction

Some 30 years ago, Davydov suggested that vibrational solitons might play a role in the energy transport of proteins [1–3]. This suggestion was guided by the observation that the hydrogen bonds that stabilize secondary structure motifs in proteins provide a nonlinearity, that together with the harmonic potentials of vibrational motions could be mathematically transferred into equations that have soliton solutions. A few years later, Careri and Scott brought the observation of a so-called anomalous band in the C=O spectrum of acetanilide (ACN), a molecular crystal that is stabilized by hydrogen bonds that mimic to some extent those in a protein (see Fig. 1), into the context of Davydov's suggestion (although we now know that this anomalous band is a vibrational polaron rather than a soliton) [4, 5].

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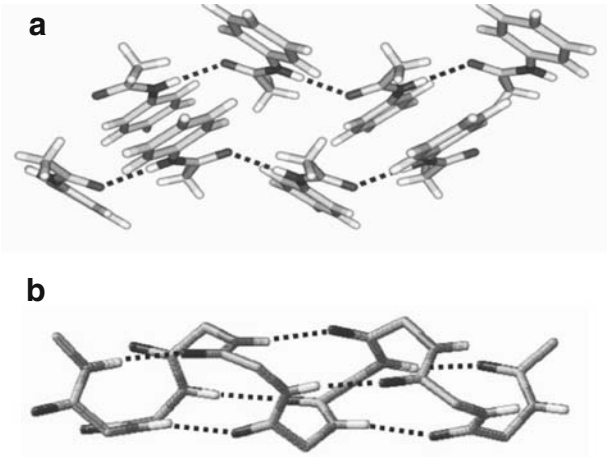

Fig. 1 Comparison of **a** crystalline acetanilide and **b** an α-helix that is part of a protein. *Dots* denote the hydrogen bond that stabilize these structures

These works of Careri and Scott triggered a hype in the field that continued until the early 1990s, the major part of which is summarized in Scott's seminal review [6]. I first learned about the field from a book, 'Davydov's Soliton Revisited' [7], which I accidentally found in my institute's library during my Ph.D. time. The book caught my interest because I was fascinated by the magic of the physical effect (which still fascinates me), its potential biological implications (in which I no longer believe), and because I felt that one could learn a great deal about vibrational solitons with the help of femtosecond vibrational spectroscopy, a relatively new technique I was involved in during my Ph.D. time.

I was initially intrigued more by the N–H band of crystalline acetanilide (Fig. 2, left), which consists of a sequence of almost-equidistant side bands. Once we had the first results from the femtosecond pump-probe experiment on this band, which directly revealed the relevant phonons that give rise to vibrational self-rapping (see Fig. 5 below), I contacted Al Scott and caught his attention right away. He invited me to visit him at the Technical University of Denmark to present my ideas and preliminary results and to discuss the problem. This 2-day visit in summer 2000 initiated an extensive and extremely instructive discussion, which went on until he tragically passed away in January 2007.

In the following paragraphs, I will briefly recapture the status of the field before we got into it (a much more comprehensive summary is given in Al Scott's review [6]). Figure 2 shows the absorption spectra of crystalline ACN in the region of the C=O and the N–H stretching vibrations. The C=O mode consists of a single peak at 1,666 cm^{-1} at room temperature, which splits into two bands with a second "anomalous" peak at 1,650 cm^{-1} at low temperatures [4]. The N–H stretching mode, on the other hand, is weakly temperature-dependent and exhibits a main peak at 3,295 cm^{-1} accompanied by an almost regular sequence of nine satellite peaks towards lower frequencies [8, 9].

The origin of the splitting of the C=O band has been the topic of many theoretical and experimental studies, including IR absorption, Raman scattering, and neutron scattering measurements [4–6, 9–16]. Careri, Scott and coworkers attributed the anomalous band to vibrational self-trapping [5, 6, 10]. In simple words, this means the following: due to excitonic interaction between the C=O groups in the regular chain of ACN molecules (Fig. 1a), these states tend to delocalize and form a vibrational exciton (vibron). However, low frequency phonons that are nonlinearly coupled to the exciton dress the latter, and

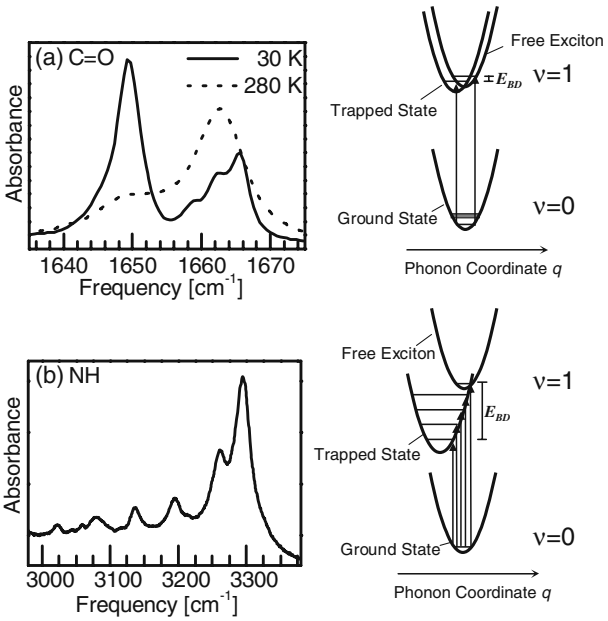

Fig. 2 Absorption spectra of **a** the C=O and **b** the N–H band of crystalline ACN and the potential energy surfaces giving rise to these spectra

thereby self-localize it. A simple theoretical description of vibrational self-trapping is obtained when exciton coupling between adjacent C=O sites is neglected in a first step (it is indeed small for ACN), leading to the displaced oscillator picture [5, 6, 12, 13]. Exciton coupling can then be reintroduced into the problem in a perturbative manner.

In the displaced oscillator picture, the energies of the $\nu = 0$ ground state and the $\nu = 1$ first excited states of the fast quantized C=O (or N–H) vibrator are modulated as a function of a slow phonon coordinate (Fig. 2, right). At zero temperature, when only the $n = 0$ phonon state is populated in the $\nu = 0$ ground state of the C=O (or N–H) vibrator, one expects to observe a Franck–Condon-like progression of absorption lines from the $\nu = 0$ ground state to the displaced $\nu = 1$ excited state with a progression spacing given by the phonon frequency. When the dimensionless displacement is small (which is the case for the C=O band in ACN), only the zero-phonon transition (i.e., the band at 1,650 cm^{-1}) carries noticeable oscillator strength, while all other transitions are weak. At higher temperatures, the $n = 0$ phonon ground state in the $\nu = 0$ C=O ground state is thermally depopulated, and the intensity of the zero-phonon line diminishes according to a $e^{-\gamma T^2}$ dependence. This is exactly what is observed for the temperature dependence of the 1650 cm^{-1} band [5, 12, 13]. This agreement was considered to be the strongest evidence for vibrational self-trapping in ACN [6]. The "normal" peak at 1666 cm^{-1} was assigned to the "free exciton" surface in Fig. 2a (right), i.e., to a surface that is not displaced, and hence does not include exciton–phonon coupling. The coexistence of these two surfaces, however, is problematic from the theoretical point of view and a topic of ongoing research (see Section 3) [17].

The N–H band of crystalline ACN has been studied much less [8, 9]. Our current picture is that the coupling mechanism is essentially the same as for the C=O band [13], except that the displacement and hence the binding energies of the self-trapped state E_{BD} are very different. In the case of the C=O band, the binding energy is smaller than one phonon quantum, while it amounts to 9 phonon quanta in the case of the N–H band (see Fig. 2).

Although this interpretation was accepted by probably a majority of the community at the time, one must mention that a couple of open questions remained. The most serious objection came from the Fermi resonance idea, viz. the accidental degeneracy of the amide I stretch mode with a combination band of an in-plane N–H band deformation as well as a torsional mode [11]. Although Raman as well as neutron scattering experiments by Barthes and collaborators largely eliminated this possibility [18, 19], the mere fact that deuteration of the C-bound hydrogens of ACN (i.e. deuteration of all hydrogens but the N–H proton) makes the anomalous peak disappear, presents yet unexplained feature that could speak in favor of a Fermi resonance. These hydrogens do not play any role in the self-trapping theory; hence, their deuteration should not matter. On the other hand, in the case of a Fermi resonance, small frequency shifts upon deuteration may very well de-tune an accidental resonance. Furthermore, the temperature *in*dependence of the N–H band is still an open, completely untackled question.

Based on this large body of work, we started to perform IR pump-probe spectroscopy on crystalline ACN to better understand the nature of the peculiarities of the C=O [20, 21] as well as the N–H [22] band, and compared the results to a closely related crystal, *N*-methylacetamide (NMA) [23]. We also studied the double peak structure of ACN theoretically [24] and extended the work to a model α-helix [25]. I will summarize the significance of the various pieces of work in the following section.

2 Pump-probe spectroscopy

In a pump-probe experiment, the various states of the system are first excited with an intense short IR laser pump pulse, and the response upon that excitation is then probed by a second short, but much weaker probe pulse. Most of the spectroscopy performed so far on the ACN problem was stationary IR absorption spectroscopy and its temperature dependence (Fig. 2). The information gained in our pump-probe experiments, as compared to stationary IR absorption spectroscopy, is manifold:

- The anharmonicities of the individual states can be measured. When pumping a state, its first excited state is populated, and the probe pulse is then probing both the upward transition to the second excited state and the downward transition back to the ground state through stimulated emission. If the state is harmonic, both upward and downward transitions appear at exactly the same frequency, but with opposite signs, and cancel each other exactly (if taking into account in addition the effect of bleaching the ground state). This statement can be extended to any set of coupled harmonic oscillators. In contrast, if the state is anharmonic, they lead to two bands with opposite signs separated by the anharmonicity of the transition (see Section 2.1). In other words, pump-probe spectroscopy is particularly sensitive to the anharmonic (nonlinear) part of the molecular potentials, whereas stationary IR absorption spectroscopy gives a signal no matter whether the state is harmonic or anharmonic.
- If two states are coupled, excitation of one state will lead to a response (e.g., a frequency shift) of the other. It shows to what extent the various transitions are entangled, or whether they can be viewed as separated problems. In addition, if pumping two or more coupled states with an ultrashort pulse, whose bandwidth covers these states simultaneously, quantum beats are observed (see Section 2.2).
- The lifetime of the pumped states can be measured with femtosecond time resolution. In this way, for example, the original idea of Davydov [2, 3] can be tested, namely

to what extent vibrational self-trapping may stabilize the excitation for timescales that would allow the energy to be made available for subsequent biological processes (see Section 2.3).

2.1 The C=O band of ACN

Figure 3 shows two pump-probe spectra obtained by excitation of either of the two absorption lines of crystalline ACN at a temperature of 90 K. The pump pulses were spectrally narrow in this experiment (spectral width ≈14 cm^{-1}) and selectively excited only one of the two bands. When resonantly pumping the "anomalous" band (1,650 cm^{-1}) of ACN, the band bleaches (negative response) and a positive band emerges at 1,644 cm^{-1}. When resonantly pumping the "normal" band (1,666 cm^{-1}), on the other hand, hardly any bleach of the band itself is observed. Only the anomalous band responds with a signal which is similar in shape, but is slightly smaller than when pumping it directly.

We have discussed the distinctly different response of both bands of ACN in detail in [20]. We start with the statement that the involved C=O vibrators are, of course, slightly anharmonic. In that sense, the "anomalous" band with a 0–1 frequency of 1,650 cm^{-1} and a 1–2 frequency of 1,644 cm^{-1} (Fig. 3, right) shows the expected anharmonic response, whereas the "normal" band at 1,666 cm^{-1} behaves strangely in that it shows no pump-probe response whatsoever. We have shown in [20] that the effective anharmonicity of excitons composed from weakly anharmonic C=O vibrators scales like its participation ratio, which is a commonly used measure of the degree of delocalization of excitonic systems [26–28]. That is, the participation is 1 for a completely localized state (localized, for example, due to disorder) and 0 for a perfectly delocalized state, i.e., a free exciton. This finding can be qualitatively explained in simple words: in a delocalized state, the oscillation amplitude of each individual site scales with $1/\sqrt{N}$, where N is the delocalization length. Hence, with increasing delocalization length N, each site is exploring a decreasingly smaller region of the potential energy surface, in which the harmonic approximation becomes increasingly more accurate. A completely delocalized state therefore will be effectively harmonic, even if the site states are slightly anharmonic. The anomalous band shows such an anharmonic response, and hence, is a localized state. The normal band, on the other hand, shows no nonlinear response, which can only be the case when it is effectively a harmonic state (it has been verified that the lifetime of the normal band is long enough to potentially observe a bleach [20]). Hence, the normal band is largely delocalized, i.e., a free exciton, in agreement with the original assignments [6].

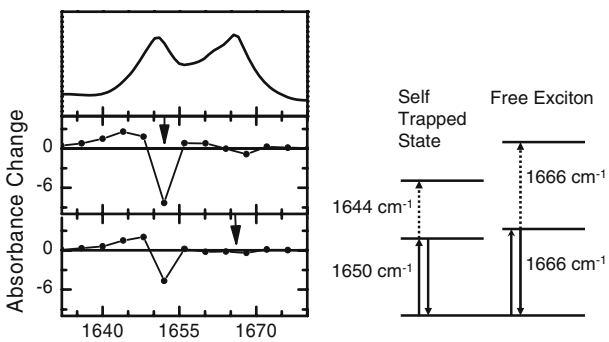

Fig. 3 *Left*: Linear absorption spectrum (*top*) and pump probe spectra of the C=O mode of crystalline ACN at 93 K for two different narrow band pump pulses chosen to be resonant with each of the absorption bands. The *arrows* mark the center frequency of the pump pulse. *Right*: Level scheme of the system, explaining the distinctively different response of both modes. Adapted from [20]

In an extension of this work, 2D-IR spectroscopy has been applied to ultimately clarify the origin of the anomalous amide I band [21]. In such an experiment, the pump frequency is continuously scanned through the spectrum, and the response is plotted as a function of both pump and probe frequencies. 2D-IR spectroscopy can distinguish between various kinds of nonlinearities of the molecular Hamiltonian. In Fig. 4, the 2D-IR spectrum of crystalline ACN is compared with that of two other molecular systems: (a) benzoylchloride and (b) *N*-methylacetamide dissolved in methanol. The stationary IR absorption spectra exhibit the same doublet structure in all three cases; however, the 2D-IR spectra differ distinctively. Benzoylchloride has been chosen as a prototype example of a molecule with a strong symmetric Fermi resonance [29], whereas *N*-methylacetamide dissolved in methanol is known to exist in two spectroscopically distinguishable conformations, one fraction hydrogen bonded to the solvent and the other fraction not [30].

If the two lines in ACN originated from molecules in two different conformations or surroundings (topological defects), as has been suggested various times [9, 16], pumping of one state would not cause any response of the other state (in contrast to what is seen in the experiment). The 2D-IR spectrum would essentially be diagonal, as it is for *N*-methylacetamide dissolved in methanol (Fig. 4). On the other hand, in the case of a Fermi resonance, another often-discussed explanation of the doublet in the ACN spectrum [11], a very characteristic coupling pattern, is obtained (Fig. 4). Investigating these coupling

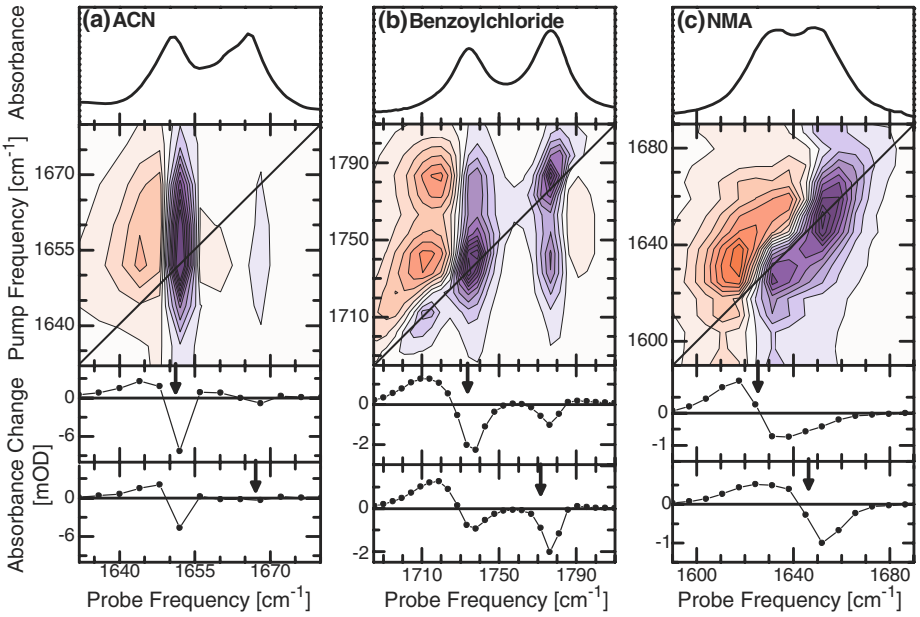

Fig. 4 Linear absorption spectra and 2D-IR pump probe spectra of the C=O mode of **a** crystalline ACN (at 93 K), **b** benzoylchloride, and **c** NMA dissolved in methanol (both at room temperature). *Blue colors* indicate negative absorption change (bleach and stimulated emission), and *red colors* positive absorption change (excited state absorption). The *two lower panels* show horizontal cuts through the 2D-IR spectrum for pump frequencies resonant with either of the two bands. The *arrows* mark the position of the pump pulse. Adapted from [21]

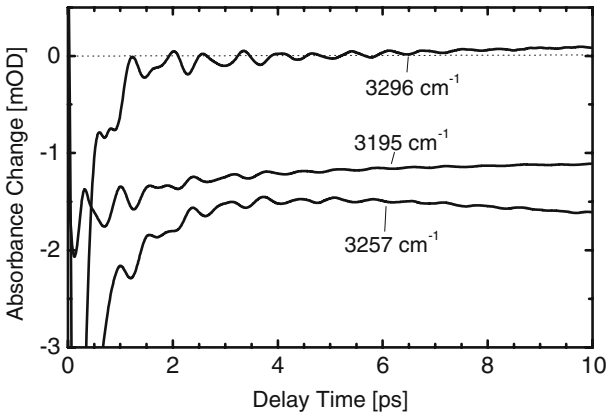

Fig. 5 Pump-probe response of the N–H band of crystalline ACN excited with an ultrashort laser pulse at various probe positions. Adapted from [22]

patterns in detail, compelling evidence against this possibility could be provided as well, and the self-trapping hypothesis could be substantiated [21].

2.2 The N–H band of ACN

Figure 5 shows the pump-probe response after exciting the N–H band of crystalline ACN [22]. In contrast to the C=O work, here we used a pump pulse so short that its bandwidth covers many of the side peaks of the N–H band. They are all exciting impulsively at the same time, leading to pronounced quantum beats in the response. A Fourier transform of the signal in Fig. 5 reveals two frequencies: a dominant peak at 48 cm^{-1} and a weaker peak at 76 cm^{-1}. We monitored the temperature dependence of these two peaks [23] and found that they coincide perfectly with the two lines in the conventional Raman spectrum (Fig. 6) [31]. This proved that the coherences indeed represent lattice phonons; in fact, this experiment identified the two phonons that mediate vibrational self-trapping in ACN.

2.3 Lifetime of the self-trapped state

After having established that the anomalous band indeed represents a self-trapped state, we may test the original hypothesis of Davydov [2, 3], namely, that vibrational self-trapping may stabilize the excitation and thereby extend its lifetime, similar to solitons in macroscopic physics. Figure 7 shows the pump-probe response of both the anomalous (1,650 cm^{-1}, filled circles) as well as of the "normal" band (1,666 cm^{-1}, open circles) of ACN after selectively exciting the former [20]. At early times, we see a bleach of only the anomalous band, which recovers on a fast 2-ps timescale. However, this relaxation is not complete, and a small negative signal remains. This indicates that the system does not relax back into the initial ground state, but into a state that is either spectroscopically dark or outside of our spectral window. On a somewhat longer timescale (35 ps), the energy still present in the crystal thermalizes. That is, the anomalous band loses intensity (a negative signal in the difference spectroscopy of Fig. 7) and the 1,666 cm^{-1} band gains intensity, exactly as in the stationary spectra of Fig. 2a when we increase the temperature. Hence, after vibrational relaxation of the initially pumped state, energy relaxes through a unknown

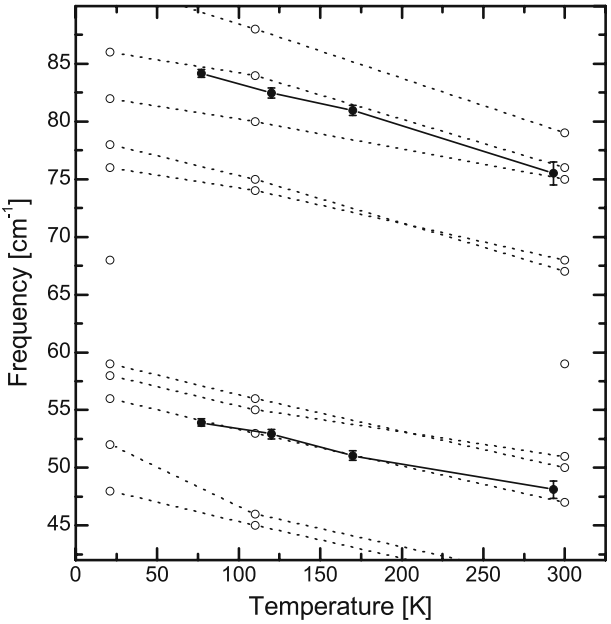

Fig. 6 Temperature dependence of the low frequency Raman modes (*open circles*) in ACN, taken from Johnston et al. [31], and of the beating frequencies observed in the pump-probe experiment (*filled circles*). The temperature dependence of the beating frequencies perfectly matches that of the Raman modes. Adapted from [23]

pathway, but then reappears as heat after 35 ps. A very similar relaxation behavior has been found for the N–H band [22].

It should be noted that the 2-ps timescale is by no means any longer than what is known for typical vibrational relaxation times; however, the more than one order of magnitude separation of timescales between vibrational relaxation of the initially pumped state and complete thermalization is not observed in this form for isolated molecules in solution. Nevertheless, the timescales are many orders of magnitudes faster than what Davydov anticipated, and much too short for the effect to be of any biological relevance, at least not in the sense of Davydov's original ideas.

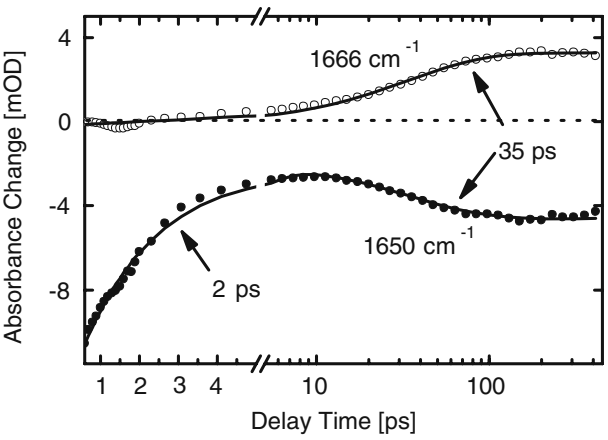

Fig. 7 Pump-probe response of the anomalous (1,650 cm^{-1}, *filled circles*) as well as of the "normal" band (1,666 cm^{-1}, *open circles*) of ACN after selectively exciting the former. Adapted from [20]

2.4 Vibrational self-trapping in other molecular crystals

Compelling evidence for vibrational self-trapping had been found only for crystalline ACN. However, the mechanism is expected to be generic and should occur in any crystal with comparable structure. In particular, one expects to observe it in NMA, which is often regarded to be *the* model compound for peptides and proteins. Both crystals, ACN and NMA, have an orthorhombic structure and consist of quasi-1D chains of hydrogen-bonded peptide units (–CO–NH–) with structural properties that are similar to those of α-helices. Nevertheless, no convincing experimental evidence for self-trapping in NMA had been found so far. In [23], we followed the strategy to transfer the knowledge we had gathered for ACN, for which vibrational self-trapping is clear and well-established, to NMA. To this end, we compared the infrared absorption spectra and the pump-probe spectra of the amide I and NH modes of acetanilide (ACN) and *N*-methylacetamide as well as their deuterated derivatives.

The amide I bands of NMA shows a temperature-dependent sideband, but it is less distinct than in ACN (Fig. 8). Also, the N–H band of NMA is accompanied by a sequence of satellite peaks, the spacings between which are larger than in ACN (which could be since NMA is lighter, and hence since lattice phonons are tentatively at higher frequencies). Comparing the pump-probe responses of these spectral anomalies in both crystals gave very similar results, providing evidence that vibrational self-trapping is indeed a common effect in hydrogen-bonded crystals.

2.5 Vibrational self-trapping in α-helices

In [25], we addressed the question of whether vibrational self-trapping can also occur in α-helices (Fig. 1b), one of the most important secondary structure motifs in proteins. We chose poly-γ-benzyl-L-glutamate (PBLG) for this investigation because it forms extremely stable, long α-helices. The monomeric unit of PBLG is a nonnatural amino acid with a long side chain that stabilizes the helix; however, the helix backbone is identical to that of natural α-helices. Because of its stability, PBLG has served as a standard model helix since the very early days of structural investigations of proteins [32].

While no anomalies were found in the amide I spectrum for this α-helix, the pump-probe response of the N–H band revealed a very uncommon but characteristic double-peak structure that can be related to bi-polarons [33–35]. A series of control experiments excluded other, more conventional explanations and showed that the existence of these

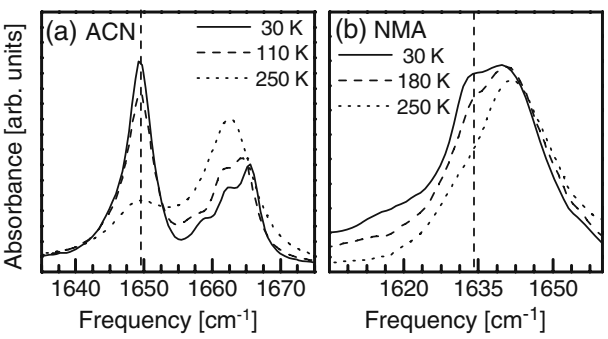

Fig. 8 IR spectrum of the amide I band of crystalline **a** ACN and **b** NMA at three different temperatures. The *vertical line* marks the position of the temperature-dependent sideband. Adapted from [23]

bi-polarons is connected to the regular folded structure of the helix. In detail, the spectroscopic signature is very different from what we have discussed in the context of crystalline ACN, mostly since acoustic rather than optical phonons are involved, but the origin is the same: nonlinear coupling of the N–H excitons to phonons along the α-helix. Woutersen and coworkers have recently observed a similar spectroscopic signature for β-sheet structures (Woutersen, private communication, paper in preparation) and explained them in the same context [36].

Tackling the problem from a somewhat different perspective, we have recently performed an experiment which comes very close to one originally proposed by Knox [37]: We have measured the heat conductivity of a peptide helix by depositing locally large amounts of vibrational energy at one end of the helix and putting certain isotope-labeled vibrational chromophors, which we employ as local thermometers, at various distances from the heater [38–40]. We find that the heat diffusivity along the helix only slightly exceed that into the surrounding solvent. The peptide helix is not a particularly good heat conductor.

3 Theoretical modeling

We have concluded from our pump-probe experiments [20] that the lower frequency band of crystalline ACN corresponds to a self-trapped state, while the higher frequency band relates to a free exciton. This conclusion has often been rationalized by the semiclassical version of the Holstein Hamiltonian, which is commonly used to describe vibrational self-trapping in ACN and which indeed has both these states as solutions. However, one can easily show [24] that the free exciton is not an eigenstate of full-quantum version of the Holstein Hamiltonian [41]. Hence, we are in the bizarre situation that the semiclassical Hamiltonian apparently describes the experimental results correctly, while the formally more accurate full-quantum Hamiltonian does not. In light of this discussion, it might seem that the correct result of the semiclassical approach is an *unfortunate coincidence*.

It is well known that self-trapping is a barrierless process in 1D, while it has to overcome a barrier in 3D. Hence, one might suspect that exciton-like states are, at least, meta-stable in 3D. Clearly, crystalline ACN is not a 1D system. It is 1D with respect to the hydrogen-bonded chains of ACN molecules and the C=O transition dipoles that are aligned in parallel, but there is no reason to assume that inter-chain exciton coupling is small compared to intra-chain exciton coupling. The hydrogen bonds play only a minor role in exciton coupling. Rather, exciton coupling is dominated by through-space transition dipole coupling [42, 43]. The nearest neighbor distance along the hydrogen-bonded chain is essentially the same as that between chains, which is why inter- and intra-chain couplings are expected to be of the same order of magnitude, however, with opposite signs (by the nature of the dipole–dipole coupling).

In order to resolve whether the 3D nature of the problem is responsible for the coexistence of the two solutions, we performed in [24] a numerically exact diagonalization of the full-quantum Holstein Hamiltonian, using a concept introduced recently by Trugman and coworkers [44, 45]. We find that the displaced oscillator picture describes the 1D case surprisingly well, even for large exciton coupling J. In the 3D case, in contrast, certain parameter regimes exist where the displaced oscillator picture breaks down. In this regime, the polaron ground state and polaron excited states collide and wildly redistribute their oscillator strengths, revealing a spectrum that compares reasonably well with the experimental spectrum (compare Fig. 2, top left, with Fig. 9, left). Analysis of the wavefunction (see [24]

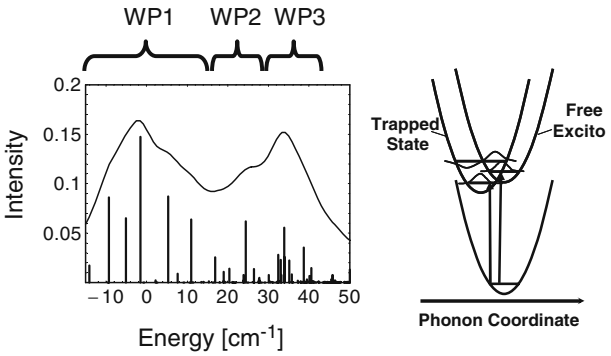

Fig. 9 Calculated absorption spectrum of the Holstein Hamiltonian in 3D with negative intra-chain coupling $J_{\parallel} = -10$ cm^{-1}, positive inter-chain coupling $J_{\perp} = +10$ cm^{-1}, phonon frequency $\omega = 50$ cm^{-1}, and exciton–phonon coupling $\chi = -25$ cm^{-1}. Stick spectra and spectra convoluted with a Lorentzian lineshape function with width 10 cm^{-1} (FWHM) are shown. The eigensates cluster in three types of states, labeled WP1, WP2 and WP3. Adapted from [24]

for details) shows that three types of states appear in this parameter regime (Fig. 9), two of which (WP1 and WP3) have the character of ground and first excited states in a displaced oscillator, while the intermediate state WP2 has the character of a free exciton which hardly couples to phonons. When going back to our initial model, these states are exactly the three states depicted in Fig. 9 (right) on the self-trapped and the free exciton surface.

However, we find that this situation occurs only in a very special parameter regime. In particular, it appears to be essential that intra- and inter-chain exciton coupling have opposite signs, which is a special property of vibrational polarons, where the source of the exciton coupling is dipole–dipole interaction. In the case of electronic polarons, for which the Holstein Hamiltonian has initially been formulated, only negative couplings have been considered [45–47]. Then, the displaced oscillator picture would remain qualitatively correct even in 3D. We can also conclude that the appearance of the double peak structure in the absorption spectrum of crystalline ACN depends relatively critically on a balance of parameters, which might explain why vibrational self-trapping is observed so clearly only in ACN, while related crystals such as NMA show, if at all, only minor effects (see Section 2.4).

4 Conclusion

Vibrational self-trapping in crystalline ACN was studied extensively in the mid-1980s through the temperature dependence of the C=O mode. Here, we apply a different approach, namely nonlinear spectroscopy. Nonlinear spectroscopy is specifically sensitive to the anharmonic part of the potential energy surface, which at the same time gives rise to nonlinear phenomena. The experiments unambiguously prove that both the N–H and the C=O bands of crystalline acetanilide (ACN), a model system for proteins, show vibrational self-trapping. The C=O band is self-trapped only at low enough temperature, while thermally-induced disorder destroys the mechanism at room temperature. The binding energy of the N–H band, on the other hand, is considerably larger, and self-trapping survives thermal fluctuations even at room temperature.

Vibrational self-trapping has been observed so far only in model crystals, while experimental evidence from polypeptides and proteins remained scarce [48, 49]. The high degree of disorder in real proteins, as compared to the perfect symmetry of a crystal, and the perturbation of surrounding solvent molecules certainly tend to destroy vibrational self-trapping. We recently provided evidence using nonlinear pump-probe spectroscopy that vibrational self-trapping does also occur in stable model-α-helices [25]. At least in the case of the N–H band, the trapping energy seems to be so high (much larger than $k_B T$) that self-trapping is indeed observable in the nonperfect environment of a real protein.

However, the lifetimes of these states are, if at all, only slightly longer than what is known for common solution phase molecular systems (in the order of 1–10 ps). Hence, it appears very questionable whether vibrational self-trapping in proteins is of any biological relevance, certainly not literally in the sense original sense proposed by Davydov, who was discussing processes which we now know to take milliseconds (e.g., the contraction of a myosin filament [1]). Hence, I do now believe that Davydov was wrong with respect to the biological relevance of Davydov's soliton, but he was in fact (more or less) right with respect to the physics. The large nonlinearity of the hydrogen bonds, which stabilize regular protein structures, gives rise to a rich variety of collective phenomena that have yet to be explored.

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